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CIHR IRSC

Microcosm-III

Message from the Scientific Director, Dr. Bhagirath Singh

Institute Mission

The mission of the Institute of Infection and Immunity (III) is to establish national leadership by setting research priorities and creating programs that promote innovative research aimed at reducing the global burden of infection and immune based diseases. The ultimate goal of such strategic research is to improve human life expectancy and the overall quality of life.

In the summer of 2002, residents of southern Ontario experienced more days of poor air quality than in any previous summer since the current monitoring system was introduced. While for most, smog represents an annoyance, for asthma sufferers, it poses a significant health risk.

Following the selection of its initial health research priorities, the Institute of Infection and Immunity (III) launched several innovative research programs to begin the process of developing these priorities into health care solutions. One of these programs addresses the thousands of children and adults suffering from asthma and allergy. The incidence of these diseases has risen rapidly in Canada and worldwide, largely, scientists believe, due to environmental factors. The suffering and the health care costs of these diseases indicate that new and bold research initiatives are required. These initiatives include finding the causes of and developing new treatments for asthma and allergy. III has developed partnerships with several other CIHR Institutes to enhance training of new asthma and allergy researchers and to take the initiative in supporting new

research teams under the umbrella of the New Emerging Teams (NET) program. In this edition and those to come, we plan to familiarize you with III-affiliated researchers and to highlight exciting research initiatives in the areas of infection and immunity.

In this edition you will also find information on the Institute's response, in collaboration with Health Canada, to new emerging health challenges in hepatitis C research, and relating to large-scale influenza vaccination in Canada. Our Institute is leading a national effort to coordinate research into safe food and water, facilitating a large-scale partnership among all the stakeholders.

I hope you enjoy the second edition of our newsletter. Your comments on this newsletter, and suggestions for future editions, are always welcome. We also welcome your input with respect to our research priorities, programs, and topics for workshops with a health research focus.

Dr. Bhagirath Singh
Scientific Director
Institute of Infection and Immunity
Canadian Institutes of Health Research

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III New Emerging Team Tackles Asthma

The third week of September represents an annual peak in illness for the millions of asthma sufferers around the world. Although smog and ragweed pollen are the likely culprits, no one is certain—and this is just another unknown confronting researchers trying to understand this

disease.

"We think we should know everything there is to know about asthma," says Dr. Moira Chan-Yeung, an asthma researcher based at the University of British Columbia. "It's a disease that's been recognized for centuries but we spend millions and millions of dollars and we're still finding

out new things each day."

Chan-Yeung is a member of a new research team studying the genetic and environmental factors that cause asthma. The team is receiving funding through the Institute of Infection and Immunity's New Emerging Teams (NET) grant program. This is the first time

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Canadian Institutes
of Health Research

Instituts de recherche
en santé du Canada

Canada

What's New at III

Strategic Funding

Hepatitis C

III and Health Canada, in response to the estimated 240,000 Canadians infected with the hepatitis C virus, have made a commitment to building research capacity in this area by launching a strategic research initiative to address the growing epidemic at several levels of research and funding.

Oculo-respiratory Syndrome (ORS)

III, on behalf of Health Canada, has requested proposals for the collection and analysis of research data from individuals who have received the influenza vaccine and suffered from ORS to assess possible side effects of repeat vaccination with the flu vaccine.

For more information, please visit our website and follow the **III Funding** link.

Annual Report

The Institute of Infection and Immunity has drafted its first annual report for the period Jan. 1, 2001 to March 31, 2002. The report will be available for general distribution and in PDF version on our website in early fall. *2

III Events

East Coast Open Forums

III's Scientific Director Dr. Bhagirath Singh presented at open forums at Dalhousie University in Halifax on Sept. 19, and at Memorial University in Newfoundland on Sept. 20. These forums engaged the research community and the public, and were an opportunity to seek input and partnerships in the development of a strong research agenda in infection and immunity.

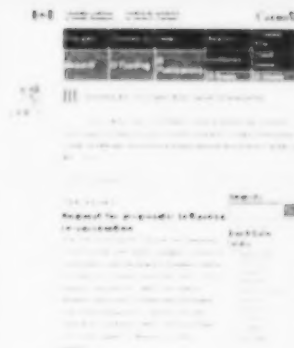
Next IAB Meeting

The next meeting of the Institute Advisory Board will take place in Ottawa, ON on Jan. 15 and 16, 2003. Please contact III Assistant Director Bruce Moor (bmoor@uwo.ca) to communicate any issues you would like brought before the board.

RFA Launch

The next cycle of Requests for Applications (RFA) will be launched in early November. These RFA will represent a large-scale commitment by III and government, research and industry partners to dealing with issues arising in food and water safety. Watch the III website for announcements and information on these and other funding opportunities. *2

On the Web



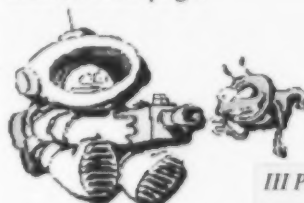
We are constantly refining and updating our website. On it you will find information about III's participation in national and international conferences, articles on III events, and information about both new and ongoing Requests for Applications. Check the **Calendar** for upcoming application deadlines. If you

haven't received our first newsletter, it can be viewed by following the **III Publications** link.

If you can suggest ways we can improve, or information you would like to see, please let us know.

Keep up to date

CIHR has launched an online sign-up feature for its mailing list that allows participants to select the Institutes from which they would like to receive updates. Register from our **Contact Us** page.



III Photo Contest

On the Lookout for Bugs

See our website for details

The Institute of Infection and Immunity at Work



III is Open for Business! From left, MP Joe Fontana, III Scientific Director Dr. Bhagirath Singh, MP Sue Barnes, Dean of Medicine and Dentistry Dr. Carol Herbert, and UWO VP (Research) Dr. Nils Petersen.

The Institute of Infection and Immunity (III) officially opened its doors May 3, 2002, but has already announced the results of its first round of RFA and launched a second round. For the uninitiated, here's how the RFA process works:

What are RFA?

RFA, or Requests for Applications, are used by institutes to build research capacity in strategic areas. Each RFA consists of a defined research focus combined with a specific implementation format, such as a team or training grant. Currently, institutes can launch RFA at four points annually: September, November, February and May.

What are "strategic areas?"

Funding is available from a number of established CIHR granting programs for research projects initiated by individual investigators or small groups of researchers. However, each Institute has a discrete pool of resources available for promoting research in areas identified as requiring a targeted approach. Strategic areas may have elements that are of interest to multiple institutes, to non-governmental organizations, and to government departments, and this can lead to the development of unique RFA sponsored by a number of partners. CIHR has also identified a number of major initiatives which intersect the strategic priorities of several institutes, and require resources beyond the capacity of any single institute to

support; these cross-institute strategic initiatives will stimulate RFA as well.

How does III determine strategic research areas?

The innovative approach to research embodied by CIHR means that research strength in prevalent areas is evaluated on an ongoing basis and that strategic research to develop a stronger research base in particular areas is promoted where appropriate. These strategic areas are identified and validated through extensive consultation with relevant communities and are approved by the Institute's Advisory Board. The Institute of Infection and Immunity has identified 10 areas in its initial strategic plan (please see our website, under *About the Institute*). Strategic areas must have a sufficient number of Canadian researchers with expertise to respond to a call for applications, as well as other characteristics which make them appropriate for an RFA. Example characteristics may include the potential to stimulate significant growth, the existence of stakeholders willing to become involved, the potential for the research to create a Canadian competitive niche or lead to international linkages, and the nature of the projects being such that they are not likely to be initiated by individual investigators.

How will the RFA process evolve from year to year? How can I have input into the development of future RFA?

Areas identified for strategic research initiatives will not remain static over time. While multiple RFA may be launched in existing areas where appropriate, the RFA process enables the Institute of Infection and Immunity to be proactive when new needs arise or when new technology becomes available. Novel areas may also stem from unique ideas or from a perceived need to bring researchers working independently in mutually beneficial areas together.

The Institute encourages Canadian stakeholders in areas relating to infection and immunity to provide input into this process, and will support conferences and workshops which may help define RFA targets or mechanisms. For more information, including instructions on how to apply for workshop funding, please visit our website at http://www.cihr-irsc.gc.ca/institutes/iii/index_e.shtml and explore the funding links, or contact Institute staff.

The Institute Advisory Board

...they make it possible



DR. FRANCIS PLUMMER,
MD, FRCPC

He's been living on the North American continent for almost a year now, and that's an unusual thing for Dr. Francis Plummer. In his Winnipeg office, a life-size sculpture of a wild African hog is a prominent memento of the 17 years he and his family lived in Nairobi, Kenya. There, Dr. Plummer directed a variety of University of Manitoba research projects in clinical infectious diseases and epidemiology research.

Dr. Plummer has a first-hand appreciation for the hardships faced by the people of developing countries. "My experience in Kenya... has given me the perspective that if we really want to solve these problems we have to solve them from a public health point of view, using public health tools." Dr. Plummer's rich experiences in global health issues make him a valuable asset to the Institute in its development of strategic research opportunities in that area. Having trained at the University of Manitoba, the University of Southern California, the University of Nairobi and the Centers for Disease Control in Atlanta, Dr. Plummer's experiences also make up an exceptionally broad background of research that has been recognized through many awards from both American and Canadian organizations, including a Tier 1 Canada Research Chair.

Although AIDS is a disease of pandemic proportions, the toll is particularly high in African countries. Dr. Plummer and his team have been studying Nairobi prostitutes who are resistant to the AIDS virus despite repeated exposure to it. These women may provide answers as to how such resistance arises, answers that researchers anticipate will lead to the development of vaccines against HIV.

Currently the Scientific Director General of the Health Canada National Microbiology Laboratory in Winnipeg, Man. and a professor in several departments at the University of Manitoba, Dr. Plummer appreciates his role as an IAB member for the Institute of Infection and Immunity. "It's really an opportunity to make a difference and see things that you believe in

happen," he says. "It's been really fun being involved in helping to shape the way ahead—what the future will look like."

Dr. Plummer sees the biggest challenge facing the Institute of Infection and Immunity as establishing communication links within the research community. "How do we get a feeling of belonging to an institute to our constituents? That is something that we have to figure out... it's going to be important."

MS. HELAINE SHIFF



Diabetes is a focal point in Ms. Helaine Shiff's life. Many years ago, when her young son was diagnosed with juvenile (Type 1) diabetes, she joined in the fight to find a cure—not in a laboratory, but as a founding member

of the Toronto chapter of the Juvenile Diabetes Research Foundation (JDRF), the world's largest non-governmental, not-for-profit funder of diabetes research.

Ms. Shiff feels that bringing the perspective of the community to each Institute is important. "I have found it rather interesting that I have been able to contribute, taking the public's point of view," said Ms. Shiff. Given the Institute's designation of autoimmune, with a focus on Type 1 diabetes, as one of its strategic research priorities, Ms. Shiff brings a rich background in that field to IAB discussions. Having worked often with scientists and members of the lay community on JDRF projects, Ms. Shiff says participating in similar discussions outside the realm of diabetes is familiar territory. A partner in her own fundraising and consulting firm Focus on You, Ms. Shiff has also contributed to discussions on public relations and partnership issues for IIB.

Ms. Shiff, currently a member of the JDRF International Board of Chancellors and the JDRF Canadian Board of Chancellors, calls her position on the IAB "a privilege." "The interaction of the entire committee and their commitment and fortitude has been most

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IIB's 15-member advisory board was selected to represent a broad swath of researchers, policy advisors and members of the lay community. The Institute Advisory Board (IAB) provides support and direction to the Scientific Director in aligning Institute activities with the IIB mission of establishing national priorities and leadership in research and training in the areas of infection and immunity. With these two profiles, we are pleased to begin a series of introductions of our IAB members.

A Partnership for Safe Food and Water

The microbial safety of Canada's food and water is one of the Institute of Infection and Immunity's top research priorities. To galvanize research in the area, the Institute is spearheading the formation of a national coalition dedicated to the coordination of a safe food and water research agenda for Canada. This initiative is a follow-up to the June 2000 CIHR Opportunity Fund Workshop on Food Safety at which researchers from a variety of different disciplines and sectors came together for the first time to discuss research priorities in the area.

By chance, the opportunity fund workshop took place just days after the contaminated water disaster in Walkerton, Ont. that claimed seven lives and made more than 2,000 people ill. "Thus," says Dr. Brett Finlay, one of the organizers of the workshop, "everyone had a heightened sense of awareness and an appreciation of the necessity of preventing future outbreaks." Finlay has studied food and water pathogens extensively. "I was concerned about the lack of coordination of research at all levels dealing with food and water safety," he says. While the United States has had national surveillance systems in place since 1996 to collect data on issues of food and water safety, Canada has no parallel organization. Finlay says he was also frustrated by the lack of communication and coordination between basic researchers and government and public health offices, and the lack of translation of findings into applications. At the workshop, more than 30 scientists and policy makers from Canadian universities, government agencies and industry convened for discussions that turned out to be "amazingly frank" according to Finlay.

Dr. Judith Bray, the Institute's Assistant Director,

Special Projects, has taken the workshop recommendations, which included the formation of a national research network, from their preliminary stages to their status today. The first step was a meeting held on Oct. 31, 2001 and attended by 17 representatives from the federal agriculture, health and environmental sectors, the food and water industry, and federal granting agencies. As a result of this meeting a Memorandum of Understanding (MOU) is about to be signed among 15 of the 17 members, defining an agreement to coordinate a national research agenda for food and water safety.

The parties to the MOU are now preparing a Request for Applications (RFA) for research in two related areas—the microbial safety of food and water, and antimicrobial resistance in the food chain. The RFA will lay a framework for the coordination of Canadian research by combining the strengths, resources and expertise of researchers from multiple sectors. Research teams responding to the RFA will be comprised of scientists from federal departments, universities, and possibly industry, working in collaboration. According to Bray, this represents an exciting approach to public health issues that will reduce research duplication and help to establish cooperation and partnership among these sectors.

The above RFA will extend the strategic initiatives relating to food and water safety launched by the Institute in May 2002, in collaboration with its CIHR partners and two Networks of Centres of Excellence: the Canadian Bacterial Diseases Network and the Canadian Water Network, and the Natural Sciences and Engineering Research Council.

While the United States has had national surveillance systems in place since 1996 to collect data on issues of food and water safety, Canada has no parallel organization.

The interaction of the entire committee and their commitment and fortitude has been most rewarding and enlightening for me personally."

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rewarding and enlightening for me personally," she adds.

Although she feels that III is on its way toward accomplishing its objectives in its strategic research priority areas, Ms.

Shiff says "the challenge will be to inform the Canadian public, health professionals, and scientists how we are meeting those objectives so that we are not operating in a vacuum."

Ms. Shiff's accomplishments have been amply recognized

through awards including the federal Canada Volunteer Award, metro Toronto's Canada's Birthday Achievement Award, and JDRC International's Volunteer of the Year award.

Strategic Training Initiative in Allergy and Asthma



Canada has long had a disproportionately strong impact on allergy research, says Dr. Kent HayGlass, an immunologist and a member of the New Emerging Team (NET) studying the origins of asthma in childhood. HayGlass is also head of a recently announced CIHR-sponsored strategic training initiative aimed at increasing research capacity in the areas of allergy and asthma.

HayGlass says that despite Canada's history of strength in allergy and asthma research, people are still suffering from these diseases. "We're really not a long way from where we were a hundred years ago in terms of our capacity to prevent or mitigate allergic diseases, despite the fact we know far more immunology, and far more physiology than we did a century ago." The training program proposal was created to address the shortage of research expertise in immunology in general, and in asthma and allergy research in particular. The program will bring together faculty with expertise in areas of allergy research as diverse as population health, cellular and molecular immunology, smooth muscle physiology and clinical medicine, says HayGlass. "We are going to offer our trainees a truly multidisciplinary program of research training. They will be highly competitive."

HayGlass emphasizes the interface between asthma and allergy, pointing out that the great majority of asthma sufferers is also allergic. Research in the area has often focused on either asthma or allergy, but HayGlass and his colleagues have traditionally focused on both and the relationships between them.

With both the NET and the strategic training initiative based in Winnipeg, there is potential for each to enhance the other. NET leader Dr. Allan Becker and team researcher Dr. Anita Kozyskyj are members of the training team as well. Becker believes the overlap is enormously valuable. One provides training for the other, and the other provides support and spin-off research for the basic project. "I think the collaborative overlapping environment will be enormously effective in providing a dramatic multiplier effect, and giving these individuals a much better chance of becoming established as independent investigators."

HayGlass agrees. "I think to have a successful training program you've got to have your trainees working on something that's really relevant, very publishable, interesting and important, and I think the NET fits all those criteria. We're excited!"

Strategic Training Initiative in Health Research Grants in the Areas of Infection and Immunity December 2001

Principal Investigator	Affiliation	Program Title	Sponsors * = Lead	Total award
CHUNG, Stephen W	University of British Columbia	Transplantation	Heart & Stroke Foundation of Canada, Michael Smith Foundation for Health Research, ICRH, IHSPR, III* and INMD	\$ 1,800,000
DOSMAN, James A	University of Saskatchewan	Public health and the agricultural rural ecosystem	ICR, ICRH, III and IPPH*	\$ 1,703,952
ELLEN, Richard P	University of Toronto	Cell signaling in mucosal inflammation & pain	Michael Smith Foundation for Health Research, The Arthritis Society*, ICRH, IHSPR, III, IMHA*, INMD and CIHR	\$ 1,797,256
HAYGLASS, Kent T	University of Manitoba	Allergy and asthma: From molecular regulation to population health	ICRH*, IHDCYH*, IHSPR, III* and IPPH	\$ 1,800,000
KUBES, Paul	University of Calgary	Health research: A transdisciplinary training program in diseases of immunopathogenesis and inflammation	Alberta Heritage Foundation for Medical Research, ICRH, III*, IMHA, INMD and CIHR	\$ 1,578,404
LEVY, Gary A	University of Toronto	Regenerative medicine	ICRH, III* and INMD*	\$ 1,784,368
PLUMMER, Francis A	University of Manitoba	International centre for infectious diseases training program	IAPH, III*, IPPH and CIHR	\$ 1,800,000
REITHMEIER, Reinhart A	Hospital for Sick Children (Toronto)	Structural biology of membrane proteins linked to disease	ICR, ICRH, IG*, III, INMD and INMHA	\$ 1,800,000
ROY, Paul H	Centre hospitalier de l'Université Laval (Québec)	Résistance aux agents antimicrobiens	Fonds de la recherche en santé du Québec and III*	\$ 1,638,000
SCHURR, Erwin A	Hôpital général de Montréal	Infectious diseases and autoimmunity	Fonds de la recherche en santé du Québec, IGH, III*, IMHA, IPPH and CIHR	\$ 1,800,000
TESCHKE, Kay	University of British Columbia	To bridge public health, engineering and policy research	Michael Smith Foundation for Health Research*, III, IPPH* and CIHR	\$ 1,800,000

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all seven members will be working on the same project, titled *Origins of Asthma in Childhood: The Role of Gene-Environment Interactions* (see table).

Where historically, research into asthma has focused on management of the disease, this team will focus on the causes, says team leader Dr. Allan Becker. "The bottom line is that the best we have to offer right now is control of asthma and other allergic diseases that ideally, we'd like to cure." However, the goal of this team is not to discover a cure, says Becker, but to identify factors that could be influenced to prevent asthma from developing.

Those who have never felt the suffocating grip of an asthma attack are largely unaware of how serious the disease can be. Becker, an asthma clinician, says, "That's the sad part—there's probably no disease where there's a larger disconnect between the ability to control the disease and actual control." Treatment and management of asthma is complex; a given patient must avoid all triggers, and may have up to three different inhalers.

Worse, asthma, the most common chronic disease of children, is on the rise. In the last quarter century, says Becker, the prevalence of asthma and other allergy-associated diseases has increased dramatically—but strangely only in developed countries. Because asthma is known to be strongly heritable, "the change in prevalence ought not to be due to genetic change but our belief really is that this is due to changes in our environment," says Becker.

It's long been recognized that asthma is the product of both genetic and environmental interactions, but where most research has focused on one or the other in isolation, this team will examine these factors together. Using Manitoba's health care databases, the researchers will evaluate the health care services provided to children born in 1995, such as medication, physician contact and institutional care. Children identified as having asthma will be invited to participate in the study, as will an equal number with no indication of either asthma or allergy. The children's family and environmental situations will be assessed, and dust from their homes analysed for allergens and endotoxin (a component of gram-

Seven researchers, four pillars

Dr. Allan Becker, team leader	University of Manitoba	Asthma clinician specializing in childhood asthma
Dr. Anita Kozyrskyj	Manitoba Centre for Health Policy, University of Manitoba	Epidemiology, population health
Dr. Kent HayGlass	University of Manitoba	Immunology
Dr. Michael Moffatt	University of Manitoba	Community and aboriginal health
Dr. Andrew Sandford and Dr. Peter Paré	University of British Columbia	Genetics
Dr. Moira Chan-Yeung	University of British Columbia	Environmental disease



Dr. Allan Becker, Dr. Anita Kozyrskyj, and Dr. Michael Moffatt are part of the team researching the early origins of asthma.

negative bacterial cell walls). All children will be clinically re-evaluated for asthma and allergies. Blood samples will be collected for first immunologic, and finally genetic analyses.

The NET grant will also allow the team to further investigate the grounds for the "hygiene hypothesis," which attributes the increased prevalence of asthma in developed countries to inhabitants' decreased exposure to bacteria and endotoxin, resulting in improperly developed immune responses. Within developed countries, "they found that children growing up on farms, particularly those that raise animals, have sig-

nificantly less asthma and allergies compared to children who are growing up in cities," says Chan-Yeung. Endotoxin is generally recognized as playing a role in the development of asthma in children, but the nature of this role has not been determined.

A province with a large aboriginal population, Manitoba provides the opportunity to study allergy and asthma in aboriginal children—a largely undeveloped research area. In aboriginal children of both rural and, to a lesser extent, urban

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communities, there is a lower incidence of asthma than in Caucasian communities. The researchers hope to learn not only why there is a difference, but also how to maintain it. Becker cites fears that asthma is an epidemic in the making in aboriginal communities that could reach proportions similar to the diabetes epidemic already raging there. He hopes the team will be able to figure out what the triggers are, and use this information to make changes or improvements in the aboriginal communities. Dr. Michael Moffatt is already working with the Centre for Aboriginal Health Research in Winnipeg, Man. to facilitate access to these communities, and says that the main advantage of this study to the aboriginal population will be the potential for prevention of future asthma and allergy-related illness. Dr. Andrew Sandford, who will be working on the genetic aspect of the project with Dr. Peter Paré, adds that aboriginal children could have different variants of the genes involved in causing allergy and asthma, genes that would not be found in Caucasian children.

The in-depth immunology work planned will also represent an expansion of that field in allergy and asthma research. "We'll be looking more at the cellular level," says Chan-Yeung, "for example, in the hygiene hypothesis, what kinds of cells are being activated and what's the mechanism?" As well, Dr. Anita Kozyskyj's work with the health care databases, which contain information on all of the children born in Manitoba in 1995, will identify subjects to take part in the study, as opposed to beginning with, for example, children known to have been treated for asthma by a particular clinic. Dr. Peter Paré describes this approach as very powerful, "because you can then generalize back to the whole population. It would be more representative of the general population than most studies."

Becker forecasts that the early results of the team's work will begin translating into benefits for asthma patients within the year. The team expects that a thorough analysis of the interactions among genes and the environment will take

ASTHMA FACTS

- Asthma kills approximately 500 adults and 20 children every year in Canada
- Between 10 and 20 per cent of children in Canada have asthma
- Asthma is the leading cause of emergency room visits
- Studies have shown that poor air quality increases the number of emergency room visits for asthma
- Estimates suggest that proper education could prevent more than 80 per cent of asthma-related deaths
- Estimates of the world-wide economic costs of asthma are higher than those for both tuberculosis and HIV/AIDS combined

several years, at which point it may be possible to pinpoint, prenatally or at birth, children at risk. Paré adds that in the shorter term, treatments might be tailored to individuals' genetic underpinnings for differences in their immunologic responses as asthmatics, potentially greatly increasing the precision of clinical trials and the treatment of individual patients.

Sandford says being part of the NET program is beneficial for each member of the team. "If we're thinking about which genes we should look at, it's much better that we talk to someone like Kent (HayGlass) who has a lot more in-depth knowledge of that immunology than we do." HayGlass appreciates that CIHR and IIR are supporting a research area that has such a high public profile. "It's not something obscure that my neighbour across the street would say, 'That must be nice but I haven't got a clue what you're working on.' It has tremendous relevance for all Canadians." HayGlass also appreciates being able to develop a research area where he believes there is a strong opportunity to advance the field, through taking a multidisciplinary approach.

Becker agrees, saying that the funding behind the team allows the research to be performed on a highly efficient level. "I don't think this would have happened without the request for proposals for the NET by CIHR and the Institutes, and I think that's one of the single best changes that I've seen in the approach to funding."